

C.A.S.

7.11.02

09/831,859

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L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:851123 CAPLUS

DOCUMENT NUMBER: 136:5985

TITLE: Preparation of tricyclic pyrazole derivatives as tyrosine kinase inhibitors for treatment of angiogenesis-related diseases

INVENTOR(S): Doyle, Kevin J.; Rafferty, Paul; Steele, Robert W.; Wilkins, David J.; Arnold, Lee D.; Hockley, Michael; Ericsson, Anna M.; Iwasaki, Nobuhiko; Ogawa, Nobuo

PATENT ASSIGNEE(S): Knoll G.m.b.H., Germany

SOURCE: PCT Int. Appl., 183 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087846	A2	20011122	WO 2001-US16153	20010517
WO 2001087846	A3	20020321		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

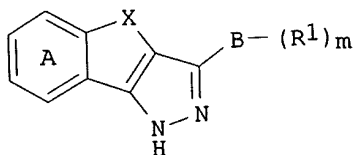
PRIORITY APPLN. INFO.:

US 2000-573366 A1 20000517

OTHER SOURCE(S):

MARPAT 136:5985

GI

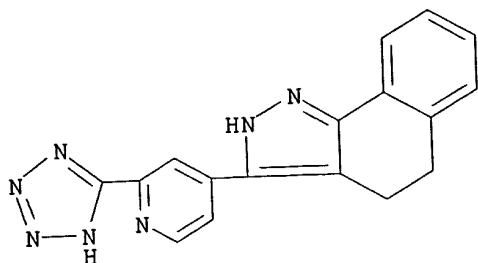


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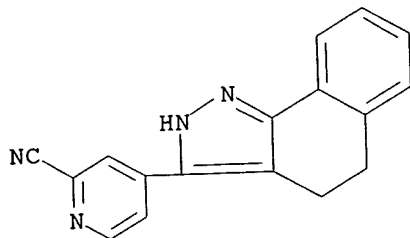
AB Title compds. I [ $m = 1-10$ ;  $X = (CH_2)_n$ , CO, O, C:NOR10, NR11,  $(CH_2)_n$ , S, SO, or SO<sub>2</sub>;  $n = 1-3$ ; R10 = alkyl; R11 = (un)substituted alkyl or Ph; B = (cyclo)alkyl, aryl, pyridyl, thienyl, furyl, or pyrrolyl; R1 = H, halo, OH, NO<sub>2</sub>, CN, hydroxyamidino, CH<sub>2</sub>NH<sub>2</sub>, formamidomethyl, (un)substituted alkenyl(oxy), alkynyl, or YW; Y = absent or alkyl, alkoxy, O, S, or CO; W = H, OH, (un)substituted Ph, alkoxy, or amino; ring A is optionally substituted with halo, OH, NO<sub>2</sub>, CN, or (un)substituted alkyl, alkoxy, PhO, carboxy, carbamoyl, amino, amido, aralkyl, alkenyl, or alkynyl; with provisoes; and racemic mixts., racemic diastereomeric mixts., tautomers, optical isomers, and pharmaceutically acceptable salts thereof] were prepd. as protein kinase inhibitors, esp. tyrosine kinase inhibitors. Thus, indan-1-one hydrazone (prepn. given) in THF at 0.degree. was treated with BuLi and then with Me 3,4,5-trimethoxybenzoate to give 3-(3,4,5-trimethoxyphenyl)-1,4-dihydroindeno[1,2-c]pyrazole. Example compds. significantly inhibited KDR kinase at concns. of .ltoreq. 50

09/831,859

.mu.M.  
IT **268563-38-8P**, 3-[2-(2H-1,2,3,4-Tetraazol-5-yl)-4-pyridyl]-4,5-dihydro-2H-benz[*g*]indazole  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of tricyclic pyrazole derivs. as tyrosine kinase inhibitors for treatment of angiogenesis-related diseases)  
RN 268563-38-8 CAPLUS  
CN 2H-Benz[*g*]indazole, 4,5-dihydro-3-[2-(1H-tetrazol-5-yl)-4-pyridinyl]-  
(9CI) (CA INDEX NAME)



IT **268564-02-9**  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reactant; prepn. of tricyclic pyrazole derivs. as tyrosine kinase inhibitors for treatment of angiogenesis-related diseases)  
RN 268564-02-9 CAPLUS  
CN 2-Pyridinecarbonitrile, 4-(4,5-dihydro-2H-benz[*g*]indazol-3-yl)- (9CI) (CA INDEX NAME)



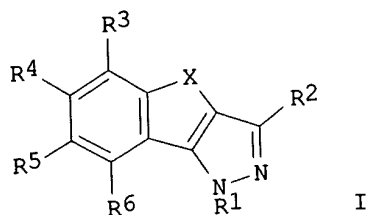
L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:335390 CAPLUS  
DOCUMENT NUMBER: 132:347566  
TITLE: Preparation of tricyclic pyrazole derivatives as protein kinase inhibitors.  
INVENTOR(S): Doyle, Kevin J.; Rafferty, Paul; Steele, Robert W.; Wilkins, David J.; Hockley, Michael; Arnold, Lee D.; Ericsson, Anna M.  
PATENT ASSIGNEE(S): Basf Aktiengesellschaft, Germany  
SOURCE: PCT Int. Appl., 210 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.

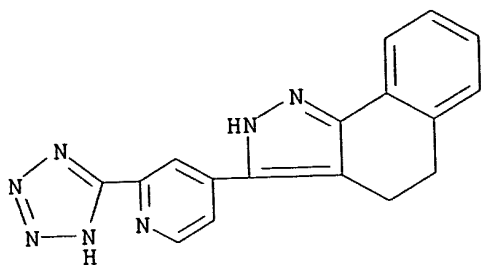
KIND DATE

APPLICATION NO. DATE

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WO 2000027822	A2	20000518	WO 1999-US26105	19991104	
WO 2000027822	A3	20000810			
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9915132	A	20010807	BR 1999-15132	19991104	
EP 1127051	A2	20010829	EP 1999-962700	19991104	
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001002219	A	20010613	NO 2001-2219	20010504	
PRIORITY APPLN. INFO.:			US 1998-107467P	P 19981106	
			WO 1999-US26105	W 19991104	
OTHER SOURCE(S):	MARPAT 132:347566				
GI					



- AB A method of inhibiting protein kinase activity comprises administration of title compds. [I; X = substituted methylene, CO, O, C:NOR7, NR8, (CH<sub>2</sub>)<sub>n</sub>, S, SO, SO<sub>2</sub>; n = 1-3; R<sub>1</sub> = H; R<sub>2</sub> = (substituted) aryl, pyridyl, thienyl, furyl, pyrrolyl; R<sub>3</sub>-R<sub>6</sub> = H, OH, halo, CO<sub>2</sub>H, alkoxycarbonyl, (substituted) alkyl, alkoxy, PhO, etc.; R<sub>7</sub> = H, alkyl; with provisos]. Thus, indan-1-one hydrazone (prepn. given) in THF at 0.degree. was treated with BuLi and then with Me 3,4,5-trimethoxybenzoate to give 3-(3,4,5-trimethoxyphenyl)-1,4-dihydroindeno[1,2-c]pyrazole.
- IT **268563-38-8P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of tricyclic pyrazole derivs. as protein kinase inhibitors)
- RN 268563-38-8 CAPLUS  
 CN 2H-Benz[g]indazole, 4,5-dihydro-3-[2-(1H-tetrazol-5-yl)-4-pyridinyl]-  
 (9CI) (CA INDEX NAME)

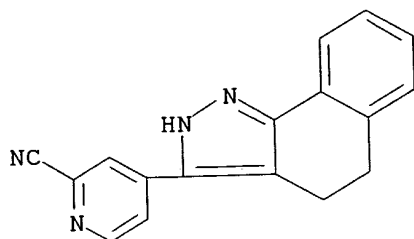


IT 268564-02-9

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of tricyclic pyrazole derivs. as protein kinase inhibitors)

RN 268564-02-9 CAPLUS

CN 2-Pyridinecarbonitrile, 4-(4,5-dihydro-2H-benz[g]indazol-3-yl)- (9CI) (CA INDEX NAME)



*Inventor*

LA ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:335255 CAPLUS  
 DOCUMENT NUMBER: 132:343312  
 TITLE: Inhibition of the formation of vascular hyperpermeability using inhibitors of KDR tyrosine kinase  
 INVENTOR(S): Arnold, Lee D.; Bousquet, Peter F.  
 PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Germany  
 SOURCE: PCT Int. Appl., 48 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027414	A2	20000518	WO 1999-US25903	19991103
WO 2000027414	A3	20000908		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
BR 9915139	A	20010807	BR 1999-15139	19991103
EP 1126842	A2	20010829	EP 1999-962685	19991103

09/831,859

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO  
NO 2001002218 A 20010618 NO 2001-2218 20010504  
US 1998-107462P P 19981106  
WO 1999-US25903 W 19991103  
PRIORITY APPLN. INFO.:

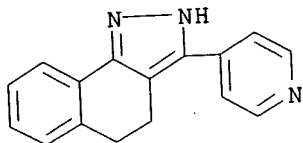
AB Vascular hyperpermeability in individuals is a prelude to a no. of  
physiol. events that are often deleterious. Among these events is the  
formation of edema, diapedesis, aberrant trans-endothelial exchange,  
extravasation, exudation and effusion, matrix deposition (often with  
abnormal stromal proliferation) and vascular hypotension. Vascular  
hyperpermeability and the subsequent events can be inhibited by the  
administration of a compd. that inhibits the enzyme activity of the VEGF  
tyrosine kinase receptor known as KDR tyrosine kinase. Preferred  
administered compds. selectively inhibit the function of KDR tyrosine  
kinase but do not block the activity of Flt-1 tyrosine kinase which is  
another VEGF tyrosine kinase receptor.

IT 80997-85-9  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(KDR tyrosine kinase inhibitors for inhibition of formation of vascular  
hyperpermeability)

RN 80997-85-9 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-3-(4-pyridinyl)-, monomethanesulfonate  
(9CI) (CA INDEX NAME)

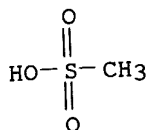
CM 1

CRN 52837-55-5  
CMF C16 H13 N3



CM 2

CRN 75-75-2  
CMF C H4 O3 S



L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:145044 CAPLUS  
DOCUMENT NUMBER: 132:204079  
TITLE: sequence and therapeutic applications for Tpl-2/cot  
kinase in relation to modulation of inflammatory  
response  
INVENTOR(S): Allen, Hamish John; Dixon, Richard Woodward; Kamens,

09/831,859

PATENT ASSIGNEE(S): Joanne Sara; Wickramasinghe, Dineli; Xu, Yajun;  
 SOURCE: Belich, Monica Polidoro; Johnston, Leland Herries;  
 Ley, Steven Charles; Salmeron, Andres  
 BASF Aktiengesellschaft, USA; Medical Research Council  
 PCT Int. Appl., 106 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000011191	A2	20000302	WO 1999-US18543	19990813
WO 2000011191	A3	20000608		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9955633	A1	20000314	AU 1999-55633	19990813
BR 9913070	A	20010508	BR 1999-13070	19990813
EP 1105501	A2	20010613	EP 1999-942203	19990813
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
NO 2001000786	A	20010417	NO 2001-786	20010216
PRIORITY APPLN. INFO.:			GB 1998-17930	A 19980818
			GB 1998-27712	A 19981216
			WO 1999-US18543	W 19990813

AB It is shown that TPL-2 is responsible for phosphorylation of p105 and its resultant proteolysis, which leads to p50 Rel translocation to the nucleus. Accordingly, the invention provides TPL-2 as a specific regulator of the activation of NF.kappa..beta., and thus as a modulator of inflammatory responses in which p105 is involved, and as a target for the development of compds. capable of influencing NF<<kapB activation. Screening assays for identifying a lead compd. for phosphorylation of the substrate MEK, p105, I.kappa.B-.alpha., I.kappa.B-.beta., MEK-1, SEK-1, NF.kappa.B. Screening assays to identify compds. that bind to the TPL-2 mol. and directly or indirectly modulate the activity of p105 are further described. These are evaluated in a cell-based assay system. Methods for identifying a lead compd. for a pharmaceutical comprising incubating a compd. to be tested with a TPL-2 mol. and tumor necrosis factor (TNF), under conditions in which, but for the presence of the compd. to be tested, the interaction of TNF and TPL-2 induces a measurable chem. or biol. effect is described. Here a reporter gene in operable linkage with a transcriptional regulatory sequence sensitive to intracellular signals transduced by TPL-2 or NF.kappa.B is included within this assay. This transcription regulatory sequence is responsive to TNF and is further explored with measuring levels of apoptosis and/or cell proliferation and/or an immune response within a cell. The test compd. is selected from a group consisting of protein based, carbohydrate based, lipid based, nucleic acid based, natural org. based, synthetically derived org. based, and antibody based compds. Treatment of a condition assocd. with NF.kappa.B induction or repression is also described. These conditions include rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, insulin-dependent diabetes mellitus, sepsis, psoriasis, misregulated TNF expression, immune system disorder, and graft rejection.

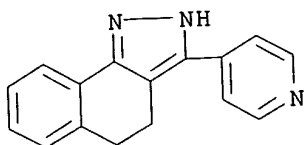
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The detn. of the effect of a test compd. on an indicator of signal transduction by the TPL-2 polypeptide is described. Lastly, antibodies are also described which are specific for TPL-2.

IT 80997-85-9  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (test compd. comprising; sequence and therapeutic applications for Tpl-2/cot kinase in relation to modulation of inflammatory response)  
RN 80997-85-9 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-3-(4-pyridinyl)-, monomethanesulfonate (9CI) (CA INDEX NAME)

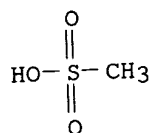
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CRN 52837-55-5  
CMF C16 H13 N3



CM 2

CRN 75-75-2  
CMF C H4 O3 S



L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:333008 CAPLUS  
DOCUMENT NUMBER: 125:127644  
TITLE: Method for obtaining improved image contrast in migration imaging members  
INVENTOR(S): Limburg, William W.; Mammino, Joseph; Liebermann, George; Griffiths, Clifford H.; Shahin, Michael M.; Malhotra, Shadi L.; Chen, Liqin; Perron, Marie-Eve  
PATENT ASSIGNEE(S): Xerox Corp., USA  
SOURCE: U.S., 147 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5514505	A	19960507	US 1995-441360	19950515
CA 2169980	AA	19961116	CA 1996-2169980	19960221

09/831,859

JP 08314240	A2	19961129	JP 1996-113456	19960508
EP 743573	A2	19961120	EP 1996-303359	19960514
EP 743573	A3	19970305		
EP 743573	B1	20000906		

R: DE, FR, GB

US 1995-441360 A 19950515

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 125:127644

AB Disclosed is a process which comprises (a) providing a migration imaging member comprising (1) a substrate and (2) a softenable layer comprising a softenable material and a photosensitive migration marking material present in the softenable layer as a monolayer of particles situated at or near the surface of the softenable layer spaced from the substrate, (b) uniformly charging the imaging member, (c) imagewise exposing the charged imaging member to activating radiation at a wavelength to which the migration marking material is sensitive, (d) causing the softenable material to soften and enabling a first portion of the migration marking material to migrate through the softenable material toward the substrate in an imagewise pattern while a second portion of the migration marking material remains substantially unmigrated within the softenable layer, and (e) contacting the second portion of the migration marking material with a transparentizing agent which transparentizes the migration marking material.

IT 80997-85-9

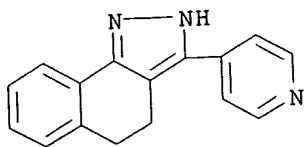
RL: DEV (Device component use); TEM (Technical or engineered material use); USES (Uses)  
(transparentizing agent for electrophotog. migration imaging members)

RN 80997-85-9 CAPLUS

CN 2H-Benz[g]indazole, 4,5-dihydro-3-(4-pyridinyl)-, monomethanesulfonate (9CI) (CA INDEX NAME)

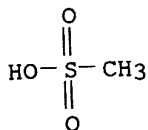
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CRN 52837-55-5  
CMF C16 H13 N3



CM 2

CRN 75-75-2  
CMF C H4 O3 S



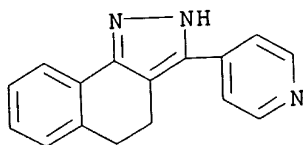
L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1975:57687 CAPLUS  
DOCUMENT NUMBER: 82:57687



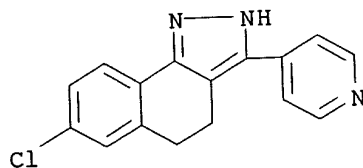
09/831,859

TITLE: Substituted indeno, naphtho, and cyclohepta pyrazoles  
INVENTOR(S): Coombs, Robert V.; Houlihan, William J.  
PATENT ASSIGNEE(S): Sandoz-Wander, Inc.  
SOURCE: U.S., 6 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

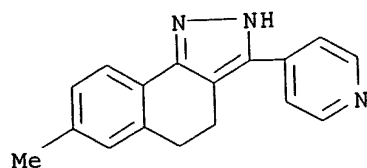
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 3843665	A	19741022	US 1973-350141	19730411
GI	For diagram(s), see printed CA Issue.				
AB	Hypotensive, contraceptive, and abortifacient (no data) pyrazoles I (R = 2-, 3-, 4-pyridyl, 2-thienyl, 2-furyl, 2-pyrrolyl, Ph, substituted phenyl; R1 = H, Cl, Me, OMe, CF3; R2 = H, OMe; R1R2 = OCH2O; n = 1,2,3) were prep'd. by treating the indanone, tetralone, or benzosuberone with RCHO and cyclizing II with p-MeC6H4-SO2NHNH2.				
IT	52837-55-5P 52837-75-9P 52837-76-0P 52837-77-1P 52837-78-2P 54752-21-5P RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)				
RN	52837-55-5 CAPLUS				
CN	2H-Benz[g]indazole, 4,5-dihydro-3-(4-pyridinyl)- (9CI) (CA INDEX NAME)				



RN 52837-75-9 CAPLUS  
CN 2H-Benz[g]indazole, 7-chloro-4,5-dihydro-3-(4-pyridinyl)- (9CI) (CA INDEX NAME)



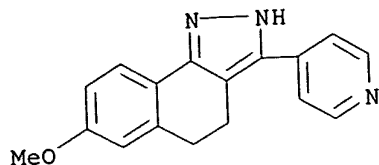
RN 52837-76-0 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-7-methyl-3-(4-pyridinyl)- (9CI) (CA INDEX NAME)



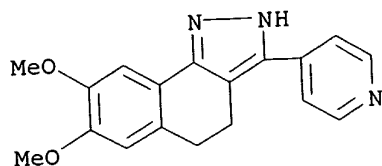
RN 52837-77-1 CAPLUS

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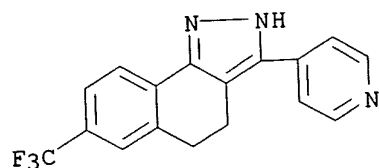
CN 2H-Benz[g]indazole, 4,5-dihydro-7-methoxy-3-(4-pyridinyl)- (9CI) (CA  
INDEX NAME)



RN 52837-78-2 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-7,8-dimethoxy-3-(4-pyridinyl)- (9CI) (CA  
INDEX NAME)



RN 54752-21-5 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-3-(4-pyridinyl)-7-(trifluoromethyl)- (9CI)  
(CA INDEX NAME)



L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1975:43412 CAPLUS  
DOCUMENT NUMBER: 82:43412  
TITLE: Substituted naphthopyrazoles  
INVENTOR(S): Habeck, Dietmar A.; Houlihan, William J.  
PATENT ASSIGNEE(S): Sandoz-Wander, Inc.  
SOURCE: U.S., 5 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3842088	A	19741015	US 1973-328402	19730131
US 3957816	A	19760518	US 1974-483626	19740627
			US 1973-328402	19730131

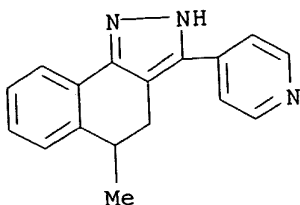
PRIORITY APPLN. INFO.:

GI For diagram(s), see printed CA Issue.

AB The naphthopyrazole I was prepd. by adding 4-pyridinecarboxaldehyde to 2-bromo-4-methyl-.alpha.-tetralone and cyclizing the spironaphthaleneoxirane II with N2H4. I inhibited fertility at 100 mg

09/831,859

s.c. twice a day.  
IT **54286-45-2P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and fertility inhibiting activity of)  
RN 54286-45-2 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-5-methyl-3-(4-pyridinyl)- (9CI) (CA INDEX NAME)



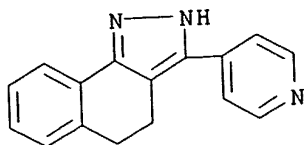
L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1974:425661 CAPLUS  
DOCUMENT NUMBER: 81:25661  
TITLE: Benzocyclohepta[1,2-c]pyrazoles, indeno[1,2-c]pyrazoles, and naphtho[1,2-c]pyrazoles  
Habeck, Dietmar A.; Houlihan, William J.  
INVENTOR(S): Sandoz Ltd.  
PATENT ASSIGNEE(S): Ger. Offen., 22 pp. Addn. to Ger. Offen. 2,249,644  
SOURCE: (CA 79;18707b).  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2317716	A1	19740502	DE 1973-2317716	19730409
NL 7304722	A	19740502	NL 1973-4722	19730405
DD 105225	W	19740412	DD 1973-169993	19730406
BE 797964	A4	19731009	BE 1973-129814	19730409
BE 806671	A4	19740429	BE 1973-137196	19731029
PRIORITY APPLN. INFO.:			US 1972-302595	19721031
			BE 1972-789948	19721011
			US 1973-341392	19730315

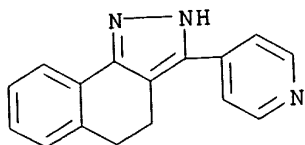
GI For diagram(s), see printed CA Issue.  
AB Addn. to Ger. Offen. 2,249,644 (CA 79: 18707b). About 40 pyrazoles (I, n = 1, 2, or 3; R = e.g. 2-, 3-, or 4-pyridyl, 2-pyrrolyl, 2-furyl, 2-thienyl, C<sub>6</sub>H<sub>4</sub>OMe-4, C<sub>6</sub>H<sub>4</sub>CF<sub>3</sub>-3, C<sub>6</sub>H<sub>3</sub>-(OMe)<sub>2</sub>-3,4, or C<sub>6</sub>H<sub>4</sub>Cl-4; R<sub>1</sub> = H, Cl, Me, or MeO; R<sub>2</sub> = H or MeO; or R<sub>1</sub>R<sub>2</sub> = OCH<sub>2</sub>O) and their hydrochlorides, useful as antihypertensives or fertility inhibitors, were prepd. by cyclization of the hydrazones II in MeONa and diglyme or in NaOH and hexane.

IT **52837-55-5P 52837-56-6P 52837-75-9P**  
**52837-76-0P 52837-77-1P 52837-78-2P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)  
RN 52837-55-5 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-3-(4-pyridinyl)- (9CI) (CA INDEX NAME)

09/831,859

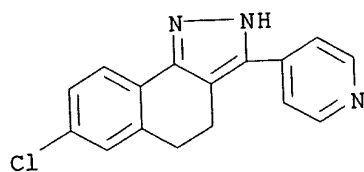


RN 52837-56-6 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-3-(4-pyridinyl)-, hydrochloride (9CI) (CA  
INDEX NAME)

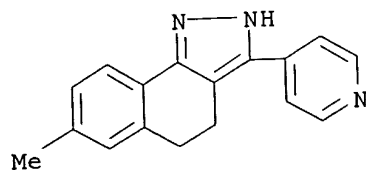


● x HCl

RN 52837-75-9 CAPLUS  
CN 2H-Benz[g]indazole, 7-chloro-4,5-dihydro-3-(4-pyridinyl)- (9CI) (CA INDEX  
NAME)

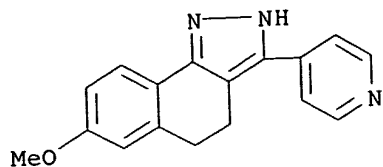


RN 52837-76-0 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-7-methyl-3-(4-pyridinyl)- (9CI) (CA INDEX  
NAME)

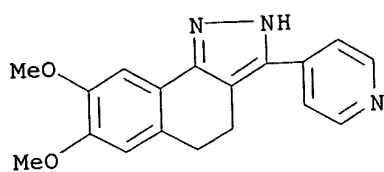


RN 52837-77-1 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-7-methoxy-3-(4-pyridinyl)- (9CI) (CA  
INDEX NAME)

09/831,859



RN 52837-78-2 CAPLUS  
CN 2H-Benz[g]indazole, 4,5-dihydro-7,8-dimethoxy-3-(4-pyridinyl)- (9CI) (CA  
INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 17:03:02 ON 11 JUL 2002)

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L2

11 S L1 FULL

L3

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L4

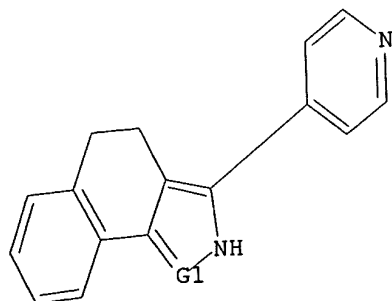
8 S L3

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L1 HAS NO ANSWERS

L1

STR



G1 C,N

Structure attributes must be viewed using STN Express query preparation.

=> s kdr

L5 1346 KDR

=>

09/831,859

---Logging off of STN---

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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS

SINCE FILE  
ENTRY  
37.53

TOTAL  
SESSION  
178.02

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE  
ENTRY  
-4.96

TOTAL  
SESSION  
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CA SUBSCRIBER PRICE

STN INTERNATIONAL LOGOFF AT 17:05:35 ON 11 JUL 2002

09/831,859

C.A.S-

7.12-02

=&gt; d ibib abs hitstr 1-3

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:335255 CAPLUS  
 DOCUMENT NUMBER: 132:343312  
 TITLE: Inhibition of the formation of vascular hyperpermeability using inhibitors of KDR tyrosine kinase  
 INVENTOR(S): Arnold, Lee D.; Bousquet, Peter F.  
 PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Germany  
 SOURCE: PCT Int. Appl., 48 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027414	A2	20000518	WO 1999-US25903	19991103
WO 2000027414	A3	20000908		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
BR 9915139	A	20010807	BR 1999-15139	19991103
EP 1126842	A2	20010829	EP 1999-962685	19991103
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
NO 2001002218	A	20010618	NO 2001-2218	20010504
PRIORITY APPLN. INFO.:			US 1998-107462P	P 19981106
			WO 1999-US25903	W 19991103

AB Vascular hyperpermeability in individuals is a prelude to a no. of physiol. events that are often deleterious. Among these events is the formation of edema, diapedesis, aberrant trans-endothelial exchange, extravasation, exudation and effusion, matrix deposition (often with abnormal stromal proliferation) and vascular hypotension. Vascular hyperpermeability and the subsequent events can be inhibited by the administration of a compd. that inhibits the enzyme activity of the VEGF tyrosine kinase receptor known as KDR tyrosine kinase. Preferred administered compds. selectively inhibit the function of KDR tyrosine kinase but do not block the activity of Flt-1 tyrosine kinase which is another VEGF tyrosine kinase receptor.

IT **80997-85-9**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(KDR tyrosine kinase inhibitors for inhibition of formation of vascular hyperpermeability)

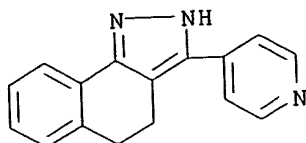
RN 80997-85-9 CAPLUS  
 CN 2H-Benz[g]indazole, 4,5-dihydro-3-(4-pyridinyl)-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 52837-55-5

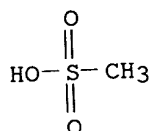
09/831,859

CMF C16 H13 N3



CM 2

CRN 75-75-2  
CMF C H4 O3 S



L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:145044 CAPLUS  
DOCUMENT NUMBER: 132:204079  
TITLE: sequence and therapeutic applications for Tpl-2/cot  
kinase in relation to modulation of inflammatory  
response  
INVENTOR(S): Allen, Hamish John; Dixon, Richard Woodward; Kamens,  
Joanne Sara; Wickramasinghe, Dineli; Xu, Yajun;  
Belich, Monica Polidoro; Johnston, Leland Herries;  
Ley, Steven Charles; Salmeron, Andres  
PATENT ASSIGNEE(S): BASF Aktiengesellschaft, USA; Medical Research Council  
SOURCE: PCT Int. Appl., 106 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000011191	A2	20000302	WO 1999-US18543	19990813
WO 2000011191	A3	20000608		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9955633	A1	20000314	AU 1999-55633	19990813
BR 9913070	A	20010508	BR 1999-13070	19990813
EP 1105501	A2	20010613	EP 1999-942203	19990813
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			



NO 2001000786 A 20010417 NO 2001-786 20010216  
 PRIORITY APPLN. INFO.: GB 1998-17930 A 19980818  
 GB 1998-27712 A 19981216  
 WO 1999-US18543 W 19990813

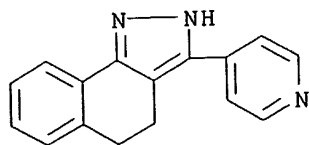
AB It is shown that TPL-2 is responsible for phosphorylation of p105 and its resultant proteolysis, which leads to p50 Rel translocation to the nucleus. Accordingly, the invention provides TPL-2 as a specific regulator of the activation of NF.kappa..beta., and thus as a modulator of inflammatory responses in which p105 is involved, and as a target for the development of compds. capable of influencing NF<<kapB activation. Screening assays for identifying a lead compd. for phosphorylation of the substrate MEK, p105, I.kappa.B-.alpha., I.kappa.B-.beta., MEK-1, SEK-1, NF.kappa.B. Screening assays to identify compds. that bind to the TPL-2 mol. and directly or indirectly modulate the activity of p105 are further described. These are evaluated in a cell-based assay system. Methods for identifying a lead compd. for a pharmaceutical comprising incubating a compd. to be tested with a TPL-2 mol. and tumor necrosis factor (TNF), under conditions in which, but for the presence of the compd. to be tested, the interaction of TNF and TPL-2 induces a measurable chem. or biol. effect is described. Here a reporter gene in operable linkage with a transcriptional regulatory sequence sensitive to intracellular signals transduced by TPL-2 or NF.kappa.B is included within this assay. This transcription regulatory sequence is responsive to TNF and is further explored with measuring levels of apoptosis and/or cell proliferation and/or an immune response within a cell. The test compd. is selected from a group consisting of protein based, carbohydrate based, lipid based, nucleic acid based, natural org. based, synthetically derived org. based, and antibody based compds. Treatment of a condition assocd. with NF.kappa.B induction or repression is also described. These conditions include rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, insulin-dependent diabetes mellitus, sepsis, psoriasis, misregulated TNF expression, immune system disorder, and graft rejection. The detn. of the effect of a test compd. on an indicator of signal transduction by the TPL-2 polypeptide is described. Lastly, antibodies are also described which are specific for TPL-2.

IT **80997-85-9**  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (test compd. comprising; sequence and therapeutic applications for Tpl-2/cot kinase in relation to modulation of inflammatory response)

RN 80997-85-9 CAPLUS  
 CN 2H-Benz[g]indazole, 4,5-dihydro-3-(4-pyridinyl)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

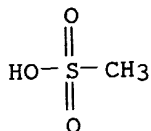
CRN 52837-55-5  
 CMF C16 H13 N3



CM 2

09/831,859

CRN 75-75-2  
CMF C H4 O3 S



L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:333008 CAPLUS  
DOCUMENT NUMBER: 125:127644  
TITLE: Method for obtaining improved image contrast in  
migration imaging members  
INVENTOR(S): Limburg, William W.; Mammino, Joseph; Liebermann,  
George; Griffiths, Clifford H.; Shahin, Michael M.;  
Malhotra, Shadi L.; Chen, Liqin; Perron, Marie-Eve  
PATENT ASSIGNEE(S): Xerox Corp., USA  
SOURCE: U.S., 147 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5514505	A	19960507	US 1995-441360	19950515
CA 2169980	AA	19961116	CA 1996-2169980	19960221
JP 08314240	A2	19961129	JP 1996-113456	19960508
EP 743573	A2	19961120	EP 1996-303359	19960514
EP 743573	A3	19970305		
EP 743573	B1	20000906		

R: DE, FR, GB  
PRIORITY APPLN. INFO.: US 1995-441360 A 19950515  
OTHER SOURCE(S): MARPAT 125:127644

AB Disclosed is a process which comprises (a) providing a migration imaging member comprising (1) a substrate and (2) a softenable layer comprising a softenable material and a photosensitive migration marking material present in the softenable layer as a monolayer of particles situated at or near the surface of the softenable layer spaced from the substrate, (b) uniformly charging the imaging member, (c) imagewise exposing the charged imaging member to activating radiation at a wavelength to which the migration marking material is sensitive, (d) causing the softenable material to soften and enabling a first portion of the migration marking material to migrate through the softenable material toward the substrate in an imagewise pattern while a second portion of the migration marking material remains substantially unmigrated within the softenable layer, and (e) contacting the second portion of the migration marking material with a transparentizing agent which transparentizes the migration marking material.

IT 80997-85-9

RL: DEV (Device component use); TEM (Technical or engineered material use); USES (Uses)  
(transparentizing agent for electrophotog. migration imaging members)

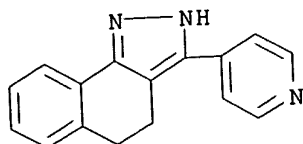
RN 80997-85-9 CAPLUS

CN 2H-Benz[g]indazole, 4,5-dihydro-3-(4-pyridinyl)-, monomethanesulfonate  
(9CI) (CA INDEX NAME)

09/831,859

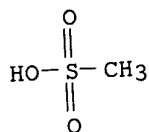
CM 1

CRN 52837-55-5  
CMF C16 H13 N3



CM 2

CRN 75-75-2  
CMF C H4 O3 S



=> s 12  
L4

2 L2

=> s 13 or 14  
L5

5 L3 OR L4

=> s vascular hyperpermeability?  
103127 VASCULAR

319 HYPERPERMEABILITY?

L6 87 VASCULAR HYPERPERMEABILITY?

(VASCULAR(W)HYPERPERMEABILITY?)

=> s 15 and 16  
L7

1 L5 AND L6

=> d

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS

AN 2000:335255 CAPLUS

DN 132:343312

TI Inhibition of the formation of **vascular hyperpermeability** using inhibitors of KDR tyrosine kinase

IN Arnold, Lee D.; Bousquet, Peter F.

PA BASF Aktiengesellschaft, Germany

SO PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

09/831,859

PI WO 2000027414 A2 20000518 WO 1999-US25903 19991103  
WO 2000027414 A3 20000908  
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,  
CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,  
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,  
MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,  
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
BR 9915139 A 20010807 BR 1999-15139 19991103  
EP 1126842 A2 20010829 EP 1999-962685 19991103  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO  
NO 2001002218 A 20010618 NO 2001-2218 20010504  
PRAI US 1998-107462P P 19981106  
WO 1999-US25903 W 19991103

=> s kdr tyrosine kinase?

1346 KDR

115896 TYROSINE

181472 KINASE?

L8 22 KDR TYROSINE KINASE?  
(KDR(W)TYROSINE(W) KINASE?)

=> s 15 and 18

L9 1 L5 AND L8

=> d

L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS

AN 2000:335255 CAPLUS

DN 132:343312

TI Inhibition of the formation of vascular hyperpermeability using inhibitors  
of **KDR tyrosine kinase**

IN Arnold, Lee D.; Bousquet, Peter F.

PA BASF Aktiengesellschaft, Germany

SO PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	WO 2000027414	A3	20000908		
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	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	BR 9915139	A	20010807	BR 1999-15139	19991103
	EP 1126842	A2	20010829	EP 1999-962685	19991103
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

09/831,859

NO 2001002218	A	20010618	NO 2001-2218	20010504
PRAI US 1998-107462P	P	19981106		
WO 1999-US25903	W	19991103		

=> d his

(FILE 'HOME' ENTERED AT 10:55:32 ON 12 JUL 2002)

FILE 'REGISTRY' ENTERED AT 10:56:55 ON 12 JUL 2002

L1	1 S 80997-85-9/RN
L2	1 S 52837-55-5/RN

FILE 'CAPLUS' ENTERED AT 10:57:57 ON 12 JUL 2002

L3	3 S L1
L4	2 S L2
L5	5 S L3 OR L4
L6	87 S VASCULAR HYPERPERMEABILITY?
L7	1 S L5 AND L6
L8	22 S KDR TYROSINE KINASE?
L9	1 S L5 AND L8

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	25.20	29.54
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-1.86	-1.86

STN INTERNATIONAL LOGOFF AT 11:00:45 ON 12 JUL 2002